Office is unable to accord to the Applicant the normal scope of claims that accompany a truly pioneering breakthrough invention.

Historically, it had been thought that gene therapy was the likely method to effect functional activity of p53 in vivo. Applicant's groundbreaking discoveries as described herein and reported in the Journal Science (at v. 286, pp. 2507-2510, and of record herein), brought immediate competitor validation and copying. Applicant's report in Science is much cited.

By way of a Supplemental Information Disclosure Statement submitted herewith, Applicant respectfully directs attention to M. Demma et al., "CP-31398 Restores DNA Binding Activity to Mutant p53 in vitro but Does not Affect p53 Homologs p63 and p73", J. Biol. Chem. v. 279, pp. 45887-45896, 2004 Internet published on August 11, 2004 as manuscript M401854200. All of the authors of this publication are employees of Schering-Plough Corporation, a pharmaceutical company that has for many years embraced the gene therapy approach to p53 therapy. It is remarkable that upon reading the present Applicant's publication in Science, Applicant's competitor immediately and extensively validated the present invention and its applicability to drug discovery. It should be noted that "CP-31398" as used in the title of the Schering-Plough publication is Applicant (i.e. Pfizer)'s very own compound identifier, and corresponds exactly to the highly effective compound X that was screened according to the very teachings of the present Specification.

In this regard, attention is again directed to Page 12 of the present application referring to Figure 6, showing testing of compound "X", N-{2-[2-(4-Methoxy-phenyl)-vinyl]-quinazolin-4-yl}-N',N'-dimethyl-propane-1,3-diamine hydrochloride. The species referred to as compound "X" is depicted in Figure 2 of the Specification, and is also the subject of *in vivo* model Example 4 (pages 49-50), and Figures 5 and 6 (see pages 11-12). Compound X of the present application **is** "CP-31398".

Attention is also directed to C. Rao et al., Abstract 2244 from the American Association for Cancer Research, 2004, reflecting studies independently sponsored from the National Cancer Institute, Bethesda, MD validating the ability of Compound X (CP-31398) to both rescue destabilized mutant p53 and promote the activity of wild-type p53. Still additional validating support for the activity of Compound X, and therefore the methodology of the present invention, is provided by the additional journal publications (also attached) of P. Stanhope-Baker et al., and J. Wischhusen et al. (which includes the Applicant herein as author). It is thus clearly apparent that those skilled in the art have recognized that the

teachings of the present invention are directed to valuable medical technology which has now been embraced for the very purpose taught by the claims solicited herein, for the treatment of cancer and for the discovery of additional organic compounds that can correct defective p53 under physiological conditions in patients.

Thus, with respect to the Examiner's objection/rejection in regard of the term "organic non-peptide compound," and the scope to be accorded thereby, Applicants respectfully submit that the present specification provides an enabling disclosure for one having ordinary skill in the art to practice the claimed invention. For example, the specification teaches that "[t]he organic non-peptide compounds of the invention can be any type of compound that, when exposed to a wild type or mutant protein of the p53 family, promote the wild type activity of the protein." (p. 17.) The specification (1) provides very numerous examples of organic non-peptide compounds which are suitable for the invention (e.g., pp. 18-31); and (2) discloses detailed methods to screen and to discover additional compounds that promote a wild-type activity of a protein of the p52 family (e.g., pp. 33-40). Thus, the present disclosure provides ample guidance to one having ordinary skill in the art to select and identify the appropriate organic non-peptide compound to practice the claimed method without undue experimentation. Applicants respectfully submit that the Examiner has no contrary evidence.

Indeed, recently, others have utilized the teachings of the present pioneering invention to identify additional organic non-peptide compounds that can bind to one or more domains of a human protein of the p53 family. For example, Bykov, et al. (WO 02/24692 A1) disclose using Applicants' procedures published in Foster, et al., Science, v. 286, pp. 2507-10 (1999) to identify such compounds. (See, e.g., pp. 20-21 of Bykov, et al.) See also the discussion of M. Demma et al. above.

Applicants respectfully submit that the Examiner's position is not supported by the law. It is well-established that any assertion by the Patent and Trademark Office that the enablement of the disclosure is not commensurate in scope with the protection sought must itself be supported by evidence or reasoning substantiating the doubts so expressed. In re Dinh-Nguyen, 181 U.S.P.Q. 46, 47 (CCPA 1974); In re Bowen, 181 U.S.P.Q. 48, 51 (CCPA 1974). The Examiner has not done so. In the present case, the Examiner has proffered no evidence or sound reasoning to support his assertion that the enabling disclosure is not commensurate in scope with the protection sought, as required by the courts.

As stated in In re Marzocchi, 169 U.S.P.Q. 367, 369 (CCPA 1971:

> As a matter of Patent Office practice then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

As a consequence, it is incumbent on the PTO to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning. Id. at 370; see also In re Brana, 51 F.3d 1560, 1566 (Fed. Cir. 1995) ("[T]he PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility."). Mere allegation by the Examiner is plainly not enough.

A specification is enabling even if it requires a "considerable amount" of experimentation, as long as the experimentation is routine. Ex parte Forman, 230 U.S.P.Q. 546, 547 (PTOB 1986); see also In re Wands, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). A major factor to be considered is whether "the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claims." Forman, 230 U.S.P.Q. at 547. As will be demonstrated below, no undue experimentation is required to carry out the claimed invention.

The Examiner also contends that, in effect, the use of organic non-peptide compounds according to the practice of the present invention also includes prior art compounds stated to be anticancer agents (see Page 11 of the Official Action in regard of the compounds disclosed by Barker et al.) However, this "connecting the dots" completely fails because even if epidermoid cancer can be associated with p53 mutations (Lee et al.), the argument simply does not take account that the Barker compounds function by blocking kinase activation/signaling via the ATP binding domain of the EGF receptor. There is neither any suggestion nor statement, other than by the Examiner, that such compound bind to p53- nor do they. Accordingly, the new art rejection should be withdrawn.

The Examiner states that "the term [organic non-peptide compound] is so broad as to include compounds that are not disclosed in the specification." Applicants respectfully submit that the Examiner's attempt to limit the scope of the claims to the specific compounds disclosed in the specification oversteps the requirements imposed by 35 U.S.C. § 112. As the court explained in In re Rainer, 134 U.S.P.Q. 343, 346 (CCPA 1962):

> It appears to us that the board is here confusing the requirements for claims with the function of the specification. One does not look to claims to find out how to practice the inventions they define, but to the specification.

The statute 35 U.S.C. § 112 does not require claims to include all of the preferred features that permit the effective function of the claimed subject matter. As the CCPA further explained in In re Borkowski, 164 U.S.P.Q. 642, 645 (CCPA 1970):

> The Examiner's approach to determining whether appellants' claims satisfy the requirements of § 112 appears to have been to study appellants' disclosure, to formulate a conclusion as to what he (the examiner) regards as the broadest invention supported by the disclosure, and then to determine whether appellants' claims are broader than the examiner's conception of what "the invention" is. We cannot agree that § 112 permits of such an approach to claims.

Applicants respectfully submit that in the present case, the Examiner has done exactly what the Court has cautioned the examiners not to do. The Examiner has limited the enabling scope of the instant disclosure by studying Applicants' disclosure, concluding that the broadest invention is supported only by the disclosed species/examples and the preferred embodiments, and impermissibly restricting the scope of the invention to what the Examiner regarded as Applicants' broadest invention.

It is well-established that claims need not be limited to exemplification or preferred embodiments in order to satisfy enablement requirements. See Ex parte Gould, 6 U.S.P.Q.2d 1680 (BPAI 1987). Further, an applicant need not provide a specific example of everything embraced by a broad claim and the PTO cannot attempt to "limit all claims to specific examples, notwithstanding the clear disclosure of a broader invention." In re Anderson, 176 U.S.P.Q. 331, 333 (CCPA 1973); See also In re Angstadt, 557 F.2d 498, 503 (CCPA 1976) (holding that "appellants are not required to disclose every species encompassed by their claims even in an unpredictable art . . . ."). Under the law, Applicants are entitled to claim all embodiments of an invention, including those that are not

specifically disclosed. U.S. v. Telectronics Inc., 8 U.S.P.Q.2d 1217, 1223 (Fed. Cir. 1988) ("the law does not require an applicant to describe in his specification every conceivable embodiment of the invention").

Moreover, as discussed in Applicants' Reply to Official Action dated January 14, 2002, Applicants are entitled to a broad claim because the present invention is pioneering as evidenced by its reception in the scientific community. See In re Hogan, 194 U.S.P.Q. 527, 537 (CCPA 1977) ("[P]ioneers . . . deserve broad claims to the broad concept").

Further, the PTO has issued patents with claims to compounds which can stabilize conformational defect in a protein. For example, U.S. Patent No. 6,270,954 (issued to Welch et al.) claims a method for improving the phenotypic defect in a cell that contains a conformationally defective target protein by contacting the cell with a "protein stabilizing agent" that is effective to improve the conformational defect. The specification support for the claimed term "protein stabilizing agent," however, is only a handful of compounds. (See, e.g., col. 8, ll. 29-41 of the '954 patent.)[1] In contrast, as discussed above, the instant specification provides substantial support for the claimed term "organic non-peptide compounds" and more than a reasonable amount of guidance to practice the claimed invention.

Applicant submits herewith a Rule 1.132 Inventor Declaration showing efficacy of a wide range of non-peptide organic compounds. The fact that numerous compounds may be inoperative is irrelevant in view of the arguments presented above, and also according to the well established principles of Atlas Powder v. E.I. duPont & Co. 750 F.2d 1569, 224 USPQ 409 (Fed. Cir 1984). What is important is that the present Applicant has disclosed a wide range of operative compounds in the as-filed application, which has readily and rapidly enabled those who have reviewed Applicant's work to promptly discover additional compounds.

In view of the foregoing remarks, Applicants respectfully submit that the Examiner's rejection under 35 U.S.C. § 112, first paragraph, is in error, and it should be withdrawn.

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1 See also U.S. Patent No. 5,900,360 (also issued to Welch, et al.) The Welch patents are based on the Brown et al. article discussed at p. 49 of the instant specification. These patents disclose administering "protein stabilizing agents" at very high doses, rendering them physiologically infeasible for treating cancer in human patients.

Conclusion

A Petition for Extension of Time (3 months) is attached in duplicate. The Patent Office is authorized to charge any fee deficiency, or credit any overpayment, to Deposit Account 16-1445. A favorable action in due course is respectfully requested.

Respectfully submitted,

Date: 3-17-05

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All of the authors of this publication are employees of Schering-Plough Corporation, a pharmaceutical company that has for many years embraced the gene therapy approach to p53 therapy. It is remarkable that upon reading the present Applicant's publication in Science, Applicant's competitor immediately and extensively validated the present invention and its applicability to drug discovery. It should be noted that "CP-31398" as used in the title of the Schering-Plough publication is Applicant (i.e. Pfizer)'s very own compound identifier, and corresponds exactly to the highly effective compound X that was screened according to the very teachings of the present Specification.

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Conclusion

An early and favorable reply is respectfully requested. The Examiner is requested to contact the undersigned so that a telephonic interview can be conducted. No fee (other than for the Supplemental IDS) is due in connection with this supplemental submission.

Respectfully submitted,

Date: 3/17/2005

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